

REMARKS

The Official Action has been carefully considered. Accordingly the amended claim presented herewith, taken with the following remarks are believed sufficient to place the application in condition for allowance.

The courteous telephone interview granted Applicants' counsel by the Examiner in charge of the application is acknowledged with appreciation. It is believed that this response is in accordance with the representations made during the interview.

In the Official Action, it is noted that an objection to claim 1 is made in paragraph 2 with respect to a typographical error in omitting the word "effects." In response to this objection, claim 1 is now revised by this amendment. The Examiner's careful reading of the claim is appreciated.

It is noted that all previous rejections against the claims have been withdrawn and new rejections made with the citation of new art. In particular, claim 1 is rejected over newly cited reference to Adawi et al. Further, claims 1, 3 and 10-12 are rejected over Kishi et al. in view of Maity et al. This is a new rejection and Kishi et al. and Maity et al. are newly applied references. Further in paragraph 3, claims 2, and 4-6 are rejected as obvious over newly cited Kishi et al. in view of newly cited Maity et al. further in view of two other references which were previously combined with other prior art.

Nevertheless, this rejection has been made Final on the grounds that Applicants amendments necessitated the new rejections. Applicants counsel recognizes that the MPEP permits rejections to be made Final under certain circumstances, but Applicants submit that a careful reading of the MPEP section 706.07(a) does not support the finality of this rejection. The rejection of unamended claims 2-12 over Kishi et al. and Maity et al. is a new

rejection of unamended claims and should not have been made final pursuant to M.P.E.P. 706.07(a). Applicants submit that the final rejection is premature and should be withdrawn and amendments made by this response should be entered.

Claim 1 stands rejected as anticipated by Adawi et al., a newly cited publication from Clinical Immunology and Immunopathology. This reference is cited by the Examiner as anticipating claim 1 on the ground that the reference teaches a method of treating radiation-induced pneumonitis and fibrosis by using an MR1 antibody via blocking Cox-2 expression. The Examiner cites Adawi et al. as teaching that MR1 greatly reduces Cox-2 expression and therefore one would have envisioned that MR1 is properly considered as a selective cox-2 inhibitor in a broad sense and thus the subject matter recited in broad claim 1 is encompassed by the teaching of this cited reference. This rejection is traversed and reconsideration is requested.

However, claim 1 is now amended to delete reference to pneumonitis as a side effect. Therefore, this rejection should now be overcome. This rejection has not been applied to any other claim.

In any event, Applicants submit that Adawi et al. do not teach or suggest what is being claimed in this application, that is, in a subject undergoing radiation treatment, administration of a selective Cox-2 inhibitor reduces one or more of the radiation side-effects. It is clearly pointed out by Adawi et al. beginning at page 227, that what MR1 accomplished from their experiment was to reduce the expression of Cox-2 in the radiation damaged lung. There is no suggestion in Adawi et al. that MRI is a selective COX-2 inhibitor. The Examiner's conclusion from this experiment that MR1 is thus a Cox-2 inhibitor is not a teaching that a selective cyclooxygenase Cox-2 inhibitor would reduce one

or more deleterious side effects of radiation treatment. Accordingly, reconsideration of this rejection is requested.

In paragraph 2, claims 1, 3 and 10-12 are rejected as unpatentable over Kishi et al. in view of Maity et al. In this rejection, the Examiner considers that Kishi et al. teach an enhancement of radiotherapy using the selective Cox-2 inhibitor celecoxib. The Examiner concludes that one would "envise that a selective Cox-2 inhibitors would reduce unwanted side effects caused by radiation therapy" based on this reference. Maity et al. is relied on as teaching that side effects such as pneumonitis which result from radiation induced injury of normal tissue could be prevented by manipulation of radiosensitivity. The Examiner concludes that one would optimize successful radiation therapy by adding selective Cox-2 inhibitors into the therapy to maximize therapeutic effectiveness by lowering unwanted side effects associated with radiation therapy. Applicants submit that the Examiner's conclusions as to what is taught by these references are clearly not based on the references themselves.

Kishi et al. relates to preferential enhancement of tumor radio response by a Cox-2 inhibitor. Contrary to the Examiner's assertions, Kishi et al. make clear that the drug, referred to as SC-236, did not appreciably alter radiation damage to cells and tissues involved in the development of radiation induced leg contractures. Further, Kishi et al. state that "The drug had no effect on radiation-induced apoptosis." (Abstract, lines 19-20). The authors conclude that the Cox-2 inhibitors have a high potential for increasing the therapeutic ratio of radiotherapy, but this has nothing to do with reducing one or more of the deleterious side effects of radiation treatment as set forth in Applicants claims. Therefore, the Examiner's conclusion that from the teaching of this reference, one would have

"envisioned that a selective Cox-2 inhibitors would reduce unwanted side effects caused by radiation therapy" is clearly not supported by the teachings of the reference.

Maity et al. says nothing about Cox-2 inhibitors. Rather Maity et al. suggest that in some tumors, apoptosis is an important mode of cell death following radiation so that agents that promote this may prove useful therapeutically. Maity et al. then states "Conversely, side effects may result from radiation induced apoptosis of normal tissues: for example pneumonitis following the destruction of endothelial cells in the pulmonary vasculature." There is nothing in this reference, however, which suggests that Cox-2 inhibitors may be used to reduce the side effects of radiation treatments. Further Maity et al. simply do not suggest what is being claimed in this application.

Further Maity et al. is inconsistent with Kishi et al. Kishi et al. makes clear that the drugs used had no effect on radiation induced apoptosis. On the other hand, Maity et al. suggest that agents that promote apoptosis may prove useful therapeutically. These are inconsistent teachings and the combination of these references clearly does not result in Applicants invention. Since the reference teachings are inconsistent, the rejection is inappropriate, Ex parte Hartman, 186 USPQ 366. Therefore, the Examiner's conclusions with respect to motivation as set forth in the second paragraph on page 4 are clearly not supported by the references themselves. Further the Examiner's final conclusion in the last sentence on page 4 is not consistent with the references and not a suggestion of Applicants invention. Therefore, reconsideration of this rejection is requested.

In paragraph 3, claims 2 and 4-6 are rejected as obvious and unpatentable over Kishi et al. as discussed above in view of Maity et al. as discussed above and further in view Ducharme et al. or Weichselbaum. This rejection is also respectfully traversed.

In lines 5 and 6 of page 5, the Examiner states "As mentioned earlier (supra), Kishi et al. in view of Maity et al. teach the method of treating side effect which occur with radiation therapy using selective Cox-2 inhibitors." For reasons pointed out above, this statement is not supported by the references themselves. These references, considered alone or in combination, do not teach the method of treating side effects which occur with radiation by the use of Cox-2 inhibitors. Further, the combination with Ducharme does not help the reference combination because Ducharme simply teaches that celecoxib is a Cox-2 inhibitor which is the subject matter of Applicants claim 3. The Weichselbaum reference adds nothing to the teaching. For reasons pointed out in Applicants previous response and in Dr. Weichselbaum's Declaration under 37 CFR 1.132, there is nothing in the Weichselbaum patent which would make it obvious to one of ordinary skill in the art to use Cox-2 inhibitors to produce one or more side effects of radiation in the side effects of those mentioned in the last paragraph on page 5 of the Official Action. For these reasons, it is submitted that this combination rejection is clearly contrary to 35 USC §103 and should be withdrawn.

On page 6, the Examiner concludes with respect to this rejection that when these references are taken together, one would have been motivated to add a selective Cox-2 inhibitor into radiation therapy to reduce dilatory side effects because Cox-2 inhibitors modulate the prostaglandin/arachidonic pathway and also potentiate tumor response to a cytotoxic agent and lower the dose of radiation. Applicants submit that these conclusions with respect to motivation are based only on the Examiner's interpretation of the references and are clearly not supported by the references themselves. As pointed out by the Federal Circuit in In re Lee, 61 USPQ 2d 1430, the references themselves must suggest the

conclusions being drawn by the patent Examiner in rejecting claims over a combination of references. Here, the Examiner has substituted her own conclusions based on knowledge of Applicants disclosure and claims. That is clearly improper and not a standard of patentability to be applied against an Applicant's claims.

The two main references, Kishi et al. and Maity et al., are inconsistent in their teachings and the secondary references do not resolve this inconsistency nor contribute to a rejection based on a combination of Kishi et al. and Maity et al. For these reasons, Applicants submit that there is no motivation to combine these references and no suggestion in these references to result in Applicants invention.

For the reasons pointed out above, it is submitted that the rejections of record are clearly in error and should be withdrawn. It is further submitted that this response is a complete response to the Official Action and serves to place the application in condition for allowance.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

MCDERMOTT, WILL & EMERY



Robert L. Price

Registration No. 22,685

600 13th Street, N.W.
Washington, DC 20005-3096
(202) 756-8000 RLP:cac
Facsimile: (202) 756-8087
Date: May 2, 2003